

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

1. (Currently amended) A method for determining *in vivo* protein activity comprising
  - a) hyperpolarising by dynamic nuclear polarisation (DNP) the NMR active nuclei of samples collected from a human or non-human animate body preadministered with at least two probe compounds each said at least two probe compounds being enriched with at least one of  $^{13}\text{C}$ -and  $^{15}\text{N}$  NMR active nuclei and wherein said at least two probe compounds influence said protein activity by acting as a substrate, inducer or inhibitor of the protein;
  - b) analysing said samples by NMR spectroscopy and generating a first NMR pattern;
  - c) hyperpolarising the NMR active nuclei of samples collected from a human or non-human animate body preadministered with said at least two probe compounds and at least one putative drug;
  - d) analysing said samples by NMR spectroscopy and hereby generating a second NMR pattern;
  - e) comparing said first and second NMR patterns thus identifying distinctions in said protein activity in said second NMR pattern which ~~w~~are due to the administration of the putative drug.
2. Cancelled.

3. Cancelled.

4. Cancelled.

5. Cancelled

6. (Previously presented) The method according to claim 1, wherein the collected samples are biofluids.

7. (Previously presented) The method according to claim 1, wherein said probe compounds are substrates, inducers or inhibitors for Cytochrome P 450 (CYP450)

8. (Previously presented) The method according to claim 7, wherein said probe compounds are substrates, inducers or inhibitors for CYP 450 isoenzymes selected from the group consisting of CYP1A2, CYP2A6, CYP2C8/9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4.

9. Cancelled

10. Cancelled.

11. (Withdrawn) A mixture comprising at least two probe compounds, all probe compounds being enriched with at least one of  $^{13}\text{C}$ - and  $^{15}\text{N}$  NMR active nuclei.

12. (Withdrawn) The mixture according to claim 11, wherein said mixture comprises at least 3 probe compounds, preferably at least 4 probe compounds.
13. (Withdrawn) The mixture according to claim 11, wherein said probe compounds are probe compounds that interact with proteins selected from the group consisting of NADPH quinone oxireductases, CYP450, N-acetyltransferase, glutathione transferase, thiomethyltransferase, thiopurine methyltransferase, sulfotransferase, UDP-glucuronosyl transferase, pseudocholinesterase, serotonin transport protein, ATP binding cassette (ABC's) and p-glycoprotein.
14. (Withdrawn) The mixture according to claim 11, wherein the mixture comprises probe compounds selected from the group consisting of phenacetin, coumarin, tolbutamide, phenytoin, mephenytoin, S-mephenytoin, bufuralol, chlorzoxazone, midazolam, caffeine, dapsone, diclofenac, debrisoquine, bupropion, antipyrine, dextromethorphan, warfarin, diazepam, alprazolam, triazolam, flurazepam, chlodiazepoxide theophylline, phenobarbital propranolol, metoprolol, labetalol, nifedipine, digitoxin, quinidine, mexiletine, lidocaine, imipramine, flurbiprofen, omeprazole, terfenadine, furafylline, codeine, nicotine, sparteine, erythromycin, benzoylcholine, butrylcholine, paraoxon, para-aminosalicylic acid, isoniazid, sulfamethazine, 5-fluorouracil, trans-stilbene oxide, D-penicillamine, captopril, ipomeanol, cyclophosphamide, halothane, zidovudine, testosterone, acetaminophen, hexobarbital, carbamazepine, cortisol, oltipraz, cyclosporin A and paclitaxel.

15. (Withdrawn) The mixture according to claim 11, wherein the mixture comprises probe compounds selected from the group consisting of sulfathiazole, dapsone, isoniazid, sulfamethoxazole, hydrazaline, caffeine and procainamide.
16. (Withdrawn) The mixture according to claim 11, wherein the mixture comprises probe compounds selected from the group consisting of phenobarbital, oltipraz and 3-methyl-cholanthrene.
17. (Withdrawn) The mixture according to claim 11, wherein the mixture comprises probe compounds selected from the group consisting of azathioprine, mercaptopurine and thioguanine.
18. (Withdrawn) The mixture according to claim 11, wherein the mixture further comprises at least one putative drug.
19. (Withdrawn) Use of the mixture according to claim 11, for the determination of *in vivo* protein activity, preferably for phenotyping.
20. (Withdrawn) Use of the mixture according to claim 18 for studying drug-drug interaction.
21. (Withdrawn) An agent for determining *in vivo* protein activity comprising a mixture comprising at least two probe compounds, all probe compounds being enriched with at least one of  $^{13}\text{C}$  and  $^{15}\text{N}$  NMR active nuclei.

22. (Withdrawn) An agent for determining *in vivo* protein activity comprising a mixture comprising at least two probe compounds, all probe compounds being enriched with at least one of  $^{13}\text{C}$  and  $^{15}\text{N}$  NMR active nuclei, for the manufacture of an agent for determining *in vivo* protein activity.
23. (Withdrawn) The mixture according to claim 21, wherein the mixture further comprises at least one putative drug.
24. Cancelled.
25. (Previously presented) The method of claim 1, wherein said probe compounds are probe compounds that are substrates, inducers or inhibitors of proteins selected from the group consisting of NADPH quinone oxireductases, CYP450, N-acetyltransferase, glutathione transferase, thiomethyltransferase, thiopurine methyltransferase, sulfotransferase, UDP-glucuronosyl transferase, pseudocholinesterase, serotonin transport protein, ATP binding cassette (ABC's) and p-glycoprotein.
26. Cancelled.
27. (Previously presented) The method of claim 7, wherein said probe compounds are selected from the group consisting of phenacetin, coumarin, tolbutamide, phenytoin, mephentoin, S-mephentoin, bufuralol, chlorzoxazone, midazolam, caffeine, dapsone, diclofenac, debrisoquine, bupropion, antipyrine, dextromethorphan, warfarin, diazepam, alprazolam, triazolam, flurazepam, chlodiazepoxide theophylline, phenobarbital propranolol, metoprolol, labetalol, nifedipine, digitoxin, quinidine,

mexiletine, lidocaine, imipramine, flurbiprofen, omeprazole, terfenadine, furafylline, codeine, nicotine, sparteine, erythromycin, benzoylcholine, butrylcholine, paraoxon, para-aminosalicylic acid, isoniazid, sulfamethazine, 5-fluorouracil, trans-stilbene oxide, D-penicillamine, captopril, ipomeanol, cyclophosphamide, halothane, zidovudine, testosterone, acetaminophen, hexobarbital, carbamazepine, cortisol, oltipraz, cyclosporin A and paclitaxel.